## WHAT IS CLAIMED IS:

- 1. An isolated infectious recombinant respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a RNA polymerase elongation factor, and a partial or complete recombinant RSV genome or antigenome having one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.
- 2. The isolated infectious recombinant RSV of claim 1, wherein said one or more shifted gene(s) or genome segment(s) is/are shifted to a more promoter-proximal or promoter-distal position by deletion or insertion of one or more displacement polynucleotide(s) within said partial or complete recombinant RSV genome or antigenome.
- 3. The isolated infectious recombinant RSV of claim 2, wherein said displacement polynucleotide(s) comprise(s) one or more polynucleotide insert(s) of between 150 nucleotides (nts) and 4,000 nucleotides in length which is inserted in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insert lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant RSV.
- 4. The isolated infectious recombinant RSV of claim 3, wherein said polynucleotide insert(s) comprises one or more RSV gene(s) or genome segment(s).
- 5. The isolated infectious recombinant RSV of claim 2, wherein said displacement polynucleotide(s) comprise(s) one or more RSV gene(s) or genome segment(s) selected from RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F and G genes and genome segments and leader, trailer and intergenic regions of the RSV genome and segments thereof.

type RSV genome or antigenome.

1	6. The isolated infectious recombinant RSV of claim 2, wherein said
2	displacement polynucleotide(s) comprise(s) one or more bovine RSV (BRSV) or human
3	RSV (HRSV) gene(s) or genome segment(s) selected from RSV NS1, NS2, N, P, M, SH,
4	M2(ORF1), M2(ORF2), L, F and G gene(s) or genome segment(s) and leader, trailer and
5	intergenic regions of the RSV genome or segments thereof.
1	7. The isolated infectious recombinant RSV of claim 6, wherein said
2	displacement polynucleotide(s) is/are deleted to form the recombinant RSV genome or
3	antigenome to cause a positional shift of said one or more shifted RSV gene(s) or genome
4	segment(s) within said recombinant genome or antigenome to a more promoter-proximal
5	position relative to a position of said RSV gene(s) or genome segment(s) within a wild

8. The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) that is/are deleted to form the recombinant RSV genome or antigenome comprise one or more RSV NS1, NS2, SH, M2(ORF2), or G gene(s) or genome segment(s) thereof.

- 9. The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV NS1 gene is deleted to form the recombinant RSV genome or antigenome.
- 10. The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV NS2 gene is deleted to form the recombinant RSV genome or antigenome.
- 11. The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV SH gene is deleted to form the recombinant RSV genome or antigenome.
- 12. The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising RSV M2(ORF2) is deleted to form the recombinant RSV genome or antigenome.

1	13. The isolated infectious recombinant RSV of claim 8, wherein a
2	displacement polynucleotide comprising a RSV G gene is deleted to form the
3	recombinant RSV genome or antigenome or antigenome.
1	14. The isolated infectious recombinant RSV of claim 8, wherein the
2	RSV F and G genes are both deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	15. The isolated infectious recombinant RSV of claim 8, wherein the
2	RSV NS1 and NS2 genes are both deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	16. The isolated infectious recombinant RSV of claim 8, wherein the
2	RSV SH and NS2 genes are both deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	17. The isolated infectious recombinant RSV of claim 8, wherein the
2	RSV SH, NS1 and NS2 genes are all deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	18. The isolated infectious recombinant RSV of claim 7, wherein said
2	displacement polynucleotide(s) comprise(s) one or more deletion(s) within a
3	nontranslated sequence at the beginning or end of an RSV open reading frame or in an
4	intergenic region or 3' leader or 5' trailer portion of the RSV genome.
1	19. The isolated infectious recombinant RSV of claim 18, wherein said
2	displacement polynucleotides comprise a partial gene deletion.
1	20. The isolated infectious recombinant RSV of claim 19, wherein said
2	partial gene deletion is a partial deletion of the SH gene.
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1	21. The isolated infectious recombinant RSV of claim 20, wherein said
2	partial deletion of the SH gene comprises a deletion within the SH downstream non-
3	translated region.

region.

1	2	The isolated infectious recombinant RSV of claim 21, which is
2	RSV 6120 havin	a deletion of 112 nucleotides at positions 4499-4610 in the
3	recombinant RS	antigenome.
1	2	The isolated infectious recombinant RSV of claim 7, wherein said
2	displacement po	nucleotide(s) is/are selected from one or more region(s) of a
3	downstream unti	slated sequence of an RSV gene.
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1	2	The isolated infectious recombinant RSV of claim 23, wherein said
2	downstream unti	slated sequence(s) is/are from NS1 (positions 519-563), NS2
3	(positions 1003-	86), P (positions 3073-3230), M (positions 4033-4197), F(positions
4	7387-7539), and	M2 (positions 8433-8490) genes.
1	2	The isolated infectious recombinant RSV of claim 7, wherein said
2	displacement po	nucleotide(s) is/are selected from one or more region(s) of a upstream
3	untranslated sequ	nce of an RSV gene.
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1	20	The isolated infectious recombinant RSV of claim 25, wherein said
2	_	am untranslated sequences is/are from NS1 (positions 55-96), NS2
3	(positions 606-6	) and/or SH (positions 4231-4300).
1	2	The inelated infections recombinent BSV of claim 7 wherein said
1		The isolated infectious recombinant RSV of claim 7, wherein said
2	-	nucleotide comprises a delection of nucleotides 4683 to 4685 of the RSV
3	G gene.	
1	2	The isolated infectious recombinant RSV of claim 7, wherein said
2		nucleotide(s) is/are selected from one or more RSV intergenic
3	sequences.	nacionac(s) is are selected from one of more ris v intergence
J	oquonoos.	
1	29	The isolated infectious recombinant RSV of claim 7, wherein said
2		nucleotide(s) is/are selected from nucleotides within the RSV 5' trailer

1 30. The isolated infectious recombinant RSV of claim 29, wherein a 2 portion of the 5' trailer region that immediately follows the L gene is reduced in size by 3 75 nucleotides, 100 nucleotides, 125 nucleotides, or more, leaving intact the 5' genomic terminus. 4 The isolated infectious recombinant RSV of claim 7, wherein said 31. displacement polynucleotide(s) is/are selected from nucleotides within the RSV 3' leader region.

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portion of the 3' trailer region that excludes a core portion of the viral promoter located within the first 11 nucleotides of the 3' leader is deleted.

The isolated infectious recombinant RSV of claim 31, wherein a

- 33. The isolated infectious recombinant RSV of claim 7, wherein a partial or complete deletion from one oxany combination of the RSV NS1, NS2, SH, F and/or M2 genes yields an adjustable reduction in genome length of between 1-806 nucleotides.
- The isolated infectious recombinant RSV of claim 7, wherein a 34. partial or complete deletion from one or any combination of RSV intergenic regions yields an adjustable reduction in genome length of between 1-198 nucleotides.
- The isolated infectious recombinant RSV of claim 7, wherein a 35. partial or complete deletion from one or any combination of RSV intergenic regions yields an adjustable reduction in genome length of between 1-198 nucleotides.
- 36. The isolated infectious recombinant RSV of claim 6\wherein said displacement polynucleotide(s) is/are added, substituted, or rearranged within the recombinant RSV genome or antigenome to cause a positional shift of said one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome to a more promoter-proximal or promoter-distal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.

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1	The isolated infectious recombinant RSV of claim 36, wherein said
2	displacement polynucleotide(s) added, substituted, or rearranged within the recombinant
3	RSV genome or antigenome comprise(s) one or more RSV NS1, NS2, SH, M2(ORF2), F,
4	and/or G gene(s) or genome segment(s) thereof.
K	38. The isolated infectious recombinant RSV of claim 36, wherein said
2	displacement polynucleotide(s) comprise(s) one or more RSV gene(s) or genome
3	segment(s) encoding one or more RSV glycoprotein(s) or immunogenic domain(s) or
4	epitope(s) thereof
1	39. The isolated infectious recombinant RSV of claim 38, wherein said
2	displacement polynucleatide(s) is/are selected from gene(s) or genome segment(s)
3	encoding RSV F, G, and/or SH glycoprotein(s) or immunogenic domain(s) or epitope(s)
4	thereof.
1	40. The isolated infectious recombinant RSV of claim 1, wherein one
2	or more RSV glycoprotein gene(s) or genome segments of RSV F, G and SH is/are
3	added, substituted or rearranged within said recombinant RSV genome or antigenome to a
4	position that is more promoter-proximal compared to a wild type gene order position of
5	said one or more RSV glycoprotein gene(s).
1	41. The isolated infectious recombinant RSV of claim 40, wherein the
2	RSV glycoprotein gene G is rearranged within said recombinant RSV genome or
3	antigenome to a gene order position that is more promoter-proximal compared to the wild
4	type gene order position of G.
1	42. The isolated infectious recombinant RSV of claim 41, wherein the
2	RSV glycoprotein gene G is shifted to gene order position 1 within said recombinant RSV
3	genome or antigenome.
1	43. The isolated infectious recombinant RSV of claim 40, wherein the

RSV glycoprotein gene F is rearranged within said recombinant RSV genome or

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antigenome to a gene order position that is more promoter-proximal compared to the wild
type gene order position of F.

- 44. The isolated infectious recombinant RSV of claim 43, wherein the RSV glycoprotein gene F is shifted to gene order position 1 within said recombinant RSV genome or antigenome.
- 45. The isolated infectious recombinant RSV of claim 40, wherein both RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or antigenome to gene order positions that are more promoter-proximal compared to the wild type gene order positions of G and F.
- 1 46. The isolated infectious recombinant RSV of claim 45, wherein the 2 RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein 3 gene F is shifted to gene order position 2 within said recombinant RSV genome or 4 antigenome.
  - 47. The isolated infectious recombinant RSV of claim 40, wherein one or more RSV NS1, NS2, SH, M2(ORF2), or G gene(s) or genome segment(s) thereof is/are deleted in the recombinant RSV genome or antigenome.
    - 48. The isolated infectious recombinant RSV of claim 40, wherein a displacement polynucleotide comprising a RSV NS1 gene is deleted to form the recombinant RSV genome or antigenome.
  - 49. The isolated infectious recombinant RSV of claim 40, wherein a displacement polynucleotide comprising a RSV NS2 gene is deleted to form the recombinant RSV genome or antigenome.
  - 50. The isolated infectious recombinant RSV of claim 40 wherein a displacement polynucleotide comprising a RSV SH gene is deleted to form the recombinant RSV genome or antigenome.
- 1 51. The isolated infectious recombinant RSV of claim 50, wherein the 2 RSV glycoprotein gene G is rearranged within said recombinant RSV genome or

G1F2/ΔSH.

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3	antigenome to a gene order position that is more promoter-proximal compared to the wil	
4	type gene order po	sition of G.
1	52.	The isolated infectious recombinant RSV of claim 51, wherein the
2	RSV glycoprotein	gene G is shifted to gene order position 1 within said recombinant RSV
3	genome or antigen	ome.
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1	<b>3</b> 3.	The isolated infectious recombinant RSV of claim 52, which is
2	G1/ΔSH.	
1	54.	The isolated infectious recombinant RSV of claim 50, wherein the
2		gene R is rearranged within said recombinant RSV genome or
3		ene order position that is more promoter-proximal compared to the wild
4	type gene order po	sition of F.
1	55.	The isolated infectious recombinant RSV of claim 54, wherein the
2	RSV glycoprotein	gene F is shifted to gene order position 1 within said recombinant RSV
3	genome or antigen	ome.
1	56.	The isolated infectious recombinant RSV of claim 55, which is
2	F1/ΔSH.	
1	57.	The isolated infectious recombinant RSV of claim 50, wherein both
2	RSV glycoprotein	genes G and F are rearranged within said recombinant RSV genome or
3	antigenome to gen	e order positions that are more promoter-proximal compared to the
4	wild type gene ord	er positions of G and F.
1	58.	The isolated infectious recombinant RSV of claim 57, wherein the
2	RSV glycoprotein	gene G is shifted to gene order position 1 and the RSV glycoprotein
3	gene F is shifted to	gene order position 2 within said recombinant RSV genome or
4	antigenome.	
1	59.	The isolated infectious recombinant RSV of claim 58, which is

G1F2/ΔNS2ΔNS2ΔSH.

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1	60.	The isolated infectious recombinant RSV of claim 40, wherein the
2	RSV SH and NS2 gen	es are both deleted to form the recombinant RSV genome or
3	antigenome or antigen	ome.
1	\\delta1.	The isolated infectious recombinant RSV of claim 60, wherein both
2	RSV glycoprotein gen	es G and F are rearranged within said recombinant RSV genome or
3	antigenome to gene or	der positions that are more promoter-proximal compared to the
4	wild type gene order p	ositions of G and F.
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1	62.	The isolated infectious recombinant RSV of claim 61, wherein the
2	RSV glycoprotein gen	e Gis shifted to gene order position 1 and the RSV glycoprotein
3	gene F is shifted to ge	ne order position 2 within said recombinant RSV genome or
4	antigenome.	
1	63.	The isolated infectious recombinant RSV of claim 62, which is
2	G1F2/ΔNS2ΔSH.	
1	64.	The isolated infectious recombinant RSV of claim 40, wherein the
2	RSV SH, NS1 and NS	2 genes are all deleted to form the recombinant RSV genome or
3	antigenome or antigen	ome.
1	65.	The isolated infectious recombinant RSV of claim 64, wherein both
2	RSV glycoprotein gen	es G and F are rearranged within said recombinant RSV genome or
3	antigenome to gene or	der positions that are more promoter-proximal compared to the
4	wild type gene order p	ositions of G and F.
1	66.	The isolated infectious recombinant RSX of claim 65, wherein the
2	RSV glycoprotein gen	e G is shifted to gene order position 1 and the RSV glycoprotein
3	gene F is shifted to gen	ne order position 2 within said recombinant RSV genome or
4	antigenome.	
1	67.	The isolated infectious recombinant RSV of claim 66, which is

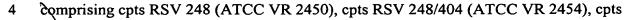
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1 68. The isolated infectious recombinant RSV of claim 1, wherein the 2 recombinant genome or antigenome comprises a partial or complete human RSV (HRSV) 3 or bovine RSV (BRSV) background genome or antigenome combined with one or more 4 heterologous gene(s) or genome segment(s) from a different RSV to form a human-5 bovine chimeric RSV genome or antigenome.

- 69. The isolated infectious recombinant RSV of claim 68, wherein the heterologous gene or genome segment is added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild type gene order position of a counterpart gene or genome segment within the partial or complete HRSV or BRSV background genome or antigenome.
- The isolated infectious recombinant RSV of claim 69, wherein both human RSV glycoprotein genes G and F are substituted at gene order positions 1 and 2, respectively, to replace counterpart G and F glycoprotein genes deleted at wild type positions 7 and 8, respectively in a partial bovine RSV background genome or antigenome.
- The isolated infectious recombinant RSV of claim 70, which is rBRSV/A2-G1F2.
- The isolated infectious recombinant RSV of claim 69, wherein one or more human RSV non-structural and/or envelope-associated genes selected from NS1, NS2, F, G, SH, and M is/are added or substituted within a partial or complete bovine RSV background genome or antigenome.
- The isolated infectious recombinant RSV of claim 69, wherein one or more human RSV envelope-associated genes selected from F, G, SH, and M is/are added or substituted within a partial bovine RSV background genome or antigenome in which one or more envelope-associated genes selected from F, G, SH, and M is/are deleted.

1	74. The isolated infections recombinant RSV of claim 73, wherein
2	human RSV envelope-associated genes F, G, and M are added within a partial bovine
3	RSV background genome or antigenome in which all of the envelope-associated genes F,
4	G, SH, and M are deleted.
×	75. The isolated infectious recombinant RSV of claim 74, which is
2	rBRSV/A2-MGR
1	76. The isolated infectious recombinant RSV of claim 69, wherein both
2	human RSV glycoprotein genes G and F are substituted at gene order positions 3 and 4,
3	respectively, to replace counterpart G and F glycoprotein genes deleted at wild type
4	positions 7 and 8, respectively in a partial bovine RSV background genome or
5	antigenome.
1	77. The isolated infectious recombinant RSV of claim 76, which is
2	rBRSV/A2-G3F4.
1	78. The isolated infectious recombinant RSV of claim 69, wherein both
2	human RSV glycoprotein genes G and F are substituted at gene order positions 1 and 2,
3	respectively, to replace counterpart G and F glycoprotein genes deleted at wild type
4	positions 7 and 8, respectively, and wherein human RSV genes NS1 and NS2 are
5	substituted for their bovine counterpart genes, in a partial bovine RSV background
6	genome or antigenome.
1	70 The inslated infectious recombinant DCV of claim 79 which is
1	79. The isolated infectious recombinant RSV of claim 78, which is
2	rBRSV/A2-G1F2NS3NS4.
1	80. The isolated infectious recombinant RSV of claim 1, in which RSV
2	M2(ORF1) is shifted to a more promoter-proximal position within the recombinant RSV
	genome or antigenome to upregulate transcription of the recombinant virus.
3	genome of antigenome to upregulate transcription of the recombinant virus.
1	81. The isolated infectious recombinant RSV of claim 1, wherein the
2	recombinant genome or antigenome incorporates at least one and up to a full complement

of attenuating mutations present within a panel of mutant human RSV strains, said panel



- 5 RSV 248/955 (ATCC VR 2453), cpts RSV 530 (ATCC VR 2452), cpts RSV 530/1009
- 6 (ATCC VR 2451), cpts RSV 530/1030 (ATCC VR 2455), RSV B-1 cp52/2B5 (ATCC
- 7 VR 2542), and RSV B-1 cp-23 (ATCC VR 2579).

82. The isolated infectious recombinant RSV of claim 81, wherein the recombinant genome or antigenome incorporates attenuating mutations adopted from different mutant RSV strains.

- 83. The isolated infectious recombinant RSV of claim 1, wherein the recombinant genome or antigenome incorporates at least one and up to a full complement of attenuating mutations specifying an amino acid substitution at Val267 in the RSV N gene, Glu218 and/or Thr523 in the RSV F gene, Asn43, Cys319, Phe 521, Gln831, Met1169, Tyr1321 and/or His 1690 in the RSV polymerase gene L, and a nucleotide substitution in the gene-start sequence of gene M2.
- 84. The isolated infectious recombinant RSV of claim 83, wherein the recombinant genome or antigenome incorporates at least two attenuating mutations.
- 85. The isolated infectious recombinant RSV of claim 83, wherein the recombinant genome or antigenome includes at least one attenuating mutation stabilized by multiple nucleotide changes in a codon specifying the mutation.
- 86. The isolated infectious recombinant RSV of claim 1, wherein the recombinant genome or antigenome further comprises a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.
- 1 87. The isolated infectious recombinant RSV of claim 86, wherein the 2 nucleotide modification alters a SH, NS1, NS2, M2ORF2, or G gene of the recombinant 3 virus.

88. The isolated infectious recombinant RSV of claim 87, wherein a SH, NS1, NS2, M2 ORF2, or G gene of the recombinant virus is deleted in whole or in part of expression of the gene is ablated by introduction of one or more stop codons in an open reading frame of the gene.

- 89. The isolated infectious recombinant RSV of claim 86, wherein the nucleotide modification comprises a nucleotide deletion, insertion, substitution, addition or rearrangement of a cis-acting regulatory sequence of a selected gene within the recombinant RSV genome or antigenome.
- 90. The isolated infectious recombinant RSV of claim 89, wherein a gene end (GE) signal of the NS1 or NS2 gene is modified.
- 91. The isolated infectious recombinant RSV of claim 89, wherein the nucleotide modification comprises an insertion, deletion, substitution, or rearrangement of a translational start site within the recombinant genome or antigenome.
- 92. The isolated infectious recombinant RSV of claim 91, wherein the translational start site for a secreted form of the RSV G glycoprotein is ablated.
- 93. The isolated infectious recombinant RSV of claim 1, wherein the recombinant genome or antigenome is modified to encode a non-RSV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting a protective immune response against said pathogen in a mammalian host.
- 1 94. The isolated infectious recombinant RSV of claim 93, which 2 incorporates one or more gene(s) and/or genome segment(s) from parainfluenza virus 3 (PIV).
- The isolated infectious recombinant RSV of claim 94, wherein the 1 95. 2 recombinant genome or antigenome encodes a HN or F glycoprotein, or an ectodomain or 3 immunogenic epitope of HN or F, of PIV1, PIV2, or PIV3.

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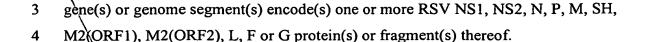
1	96. The isolated infectious recombinant RSV of claim 1 which is a
2	virus.
1	7. The isolated infectious recombinant RSV of claim 1 which is a
2	subviral particle.
$\geq_1$	98. The isolated infectious recombinant RSV of claim 2, wherein said
2	displacement polynucleotide is added within or deleted from a noncoding region of the
3	recombinant RSV genome or antigenome.
1	99. The isolated infectious recombinant RSV of claim 1, wherein the
2	recombinant genome or antigenome incorporates antigenic determinants from one or both
3	subgroup A and subgroup B human RSV.
1	100. A method for stimulating the immune system of an individual to
2	induce protection against RSV which comprises administering to the individual an
3	immunologically sufficient amount of the recombinant RSV of claim 1 combined with a
4	physiologically acceptable carrier.
1	101. The method of claim 100, wherein the recombinant RSV is
2	administered in a dose of $10^3$ to $10^6$ PFU.
1	102. The method of claim 100, wherein the recombinant RSV is
2	administered to the upper respiratory tract.
1	103. The method of claim 100, wherein the recombinant RSV is
2	administered by spray, droplet or aerosol.
1	104. The method of claim 100, wherein the recombinant RSV is
2	administered to an individual seronegative for antibodies to RSV or possessing
3	transplacentally acquired maternal antibodies to RSV.
1	105. The method of claim 100, wherein the recombinant RSV elicits an

immune response against either human RSV A or RSV B.

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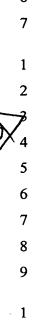
1		106.	The method of claim 100, wherein the recombinant RSV elicits an
2	immune respon	nse aga	inst both human RSV A and RSV B.
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1		107.	The method of claim 100, wherein the recombinant RSV elicits an
2	immune respon	ise aga	inst either human RSV A or RSV B and is co-administered with an
3	immunologica	lly suff	cient amount of a second attenuated RSV capable of eliciting an
4	immune respon	nse aga	inst human RSV A or RSV B, whereby an immune response is
5	elicited against	t both h	numan RSV A and RSV B.
1		108.	The method of claim 107, wherein the recombinant RSV and
2	second attenua	ted RS	V are administered simultaneously as a mixture.
1		109.	An immunogenic composition to elicit an immune response against
2	RSV comprising	ng an ii	mmunologically sufficient amount of the recombinant RSV of claim
3	1 in a physiolo	gically	acceptable carrier.
1		110.	The immunogenic composition of claim 109, formulated in a dose
2	of 10 <sup>3</sup> to 10 <sup>6</sup> P	FU.	
1		111.	The immunogenic composition of claim 109, formulated for
2	administration	to the	upper respiratory tract by spray, droplet or aerosol.
1		112.	The immunogenic composition of claim 109, wherein the
2	recombinant R	SV elic	cits an immune response against either human RSV A or RSV B or
3	both human RS	SV A a	nd RSV B.
1		113.	The isolated infectious recombinant RSV of claim 1, wherein the
2	recombinant ge	enome	or antigenome comprises a partial or complete RSV vector genome
3	or antigenome	combi	ned with one or more heterologous genes or genome segments
4	encoding one o	or more	antigenic determinants of one or more heterologous pathogens.
1		114.	The isolated infectious recombinant RSV of claim 113, wherein

said one or more heterologous pathogens is a heterologous RSV and said heterologous



115. The isolated infectious recombinant RSV of claim 113, wherein the vector genome or antigenome is a partial or complete RSV A genome or antigenome and the heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are of a RSV B subgroup virus.

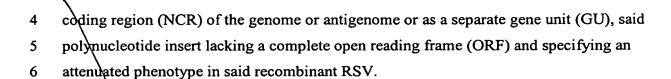
- 116. The isolated infectious recombinant RSV of claim 113, wherein the chimeric genome or antigenome incorporates one or more gene(s) or genome segment(s) of a BRSV that specifies attenuation.
- 117. The isolated infectious recombinant RSV of claim 113, wherein one or more HPIV1, HRIV2, or HPIV3 gene(s) or genome segment(s) encoding one or more HN and/or F glycoprotein(s) or antigenic domain(s), fragment(s) or epitope(s) thereof is/are added to or incorporated within the partial or complete HRSV vector genome or antigenome.
- 118. The isolated infectious recombinant RSV of claim 113, wherein the vector genome or antigenome is a partial or complete BRSV genome or antigenome and the heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are of one or more HRSV(s).
- partial or complete BRSV genome or antigenome incorporates one or more gene(s) or genome segment(s) encoding one or more HRSV glycoprotein genes selected from F, G and SH, or one or more genome segment(s) encoding cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope portion(s) of F, G, and/or SH of HRSV.
  - 120. The isolated infectious recombinant RSV of claim 113, wherein the vector genome or antigenome is a partial or complete HRSV or BRSV genome or antigenome and the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses,



6 cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses,
7 alphaviruses and influenza viruses.

121. The isolated infectious recombinant RSV of claim 120, wherein said one or more heterologous antigenic determinant(s) is/are selected from measles virus HA and F proteins, subgroup A or subgroup B respiratory syncytial virus F, G, SH and M2 proteins, mumps virus HN and F proteins, human papilloma virus L1 protein, type 1 or type 2 human immunodeficiency virus gp160 protein, herpes simplex virus and cytomegalovirus gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, and gM proteins, rabies virus G protein, Epstein Barr Virus gp350 protein; filovirus G protein, bunyavirus G protein, Flavivirus E and NS1 proteins, and alphavirus E protein, and antigenic domains, fragments and epitopes thereof.

- 122. The isolated infectious recombinant RSV of claim 121, wherein the heterologous pathogen is measles virus and the heterologous antigenic determinant(s) is/are selected from the measles virus HA and F proteins and antigenic domains, fragments and epitopes thereof.
- 123. The isolated infectious recombinant RSV of claim 122, wherein a transcription unit comprising an open reading frame (ORF) of a measles virus HA gene is added to or incorporated within a HRSV vector genome or antigenome.
- RSV genome or antigenome having one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.
- one or more shifted gene(s) or genome segment(s) is/are shifted to a more promoter-proximal position by insertion or deletion of one or more displacement polynucleotide(s) within said partial or complete recombinant RSV genome or antigenome.
- 126. The isolated polynucleotide molecule of claim 125, wherein said displacement polynucleotide(s) comprise(s) one or more polynucleotide insert(s) of between 150 nucleotides (nts) and 4,000 nucleotides in length which is inserted in a non-



- 127. The isolated polynucleotide molecule of claim 126, wherein said polynucleotide insert(s) comprises one or more RSV gene(s) or genome segment(s).
- 128. The isolated polynucleotide molecule of claim 127, wherein said displacement polynucleotide(s) comprise(s) one or more bovine RSV (BRSV) or human RSV (HRSV) gene(s) or genome segment(s) selected from RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F and G gene(s) or genome segment(s) and leader, trailer and intergenic regions of the RSV genome or segments thereof.
- 129. The isolated polynucleotide molecule of claim 128, wherein said displacement polynucleotide(s) is/are deleted to form the recombinant RSV genome or antigenome to cause a positional shift of said one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome to a more promoter-proximal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.
- 130. The isolated polynucleotide molecule of claim 129, wherein said displacement polynucleotide(s) that is are deleted to form the recombinant RSV genome or antigenome comprise one or more RSV NS1, NS2, SH, M2(ORF2), or G gene(s) or genome segment(s) thereof.
- 131. The isolated polynucleotide molecule of claim 130, wherein a displacement polynucleotide comprising a RSV NS1 gene is deleted to form the recombinant RSV genome or antigenome.
- 132. The isolated polynucleotide molecule of claim 130, wherein a displacement polynucleotide comprising a RSV NS2 gene is deleted to form the recombinant RSV genome or antigenome.
- 1 133. The isolated polynucleotide molecule of claim 130, wherein a 2 displacement polynucleotide comprising a RSV SH gene is deleted to form the 3 recombinant RSV genome or antigenome.

1	\ 134. The isolated polynucleotide molecule of claim 130, wherein a
2	displacement polynucleotide comprising RSV M2(ORF2) is deleted to form the
3	recombinant RSV genome or antigenome.
1	135. The isolated polynucleotide molecule of claim 130, wherein a
<b>7</b> 2	displacement polynucleotide comprising a RSV G gene is deleted to form the
3	recombinant RSV genome or antigenome or antigenome.
1	136. The isolated polynucleotide molecule of claim 130, wherein the
2	RSV F and G genes are both deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	137. The isolated polynucleotide molecule of claim 130, wherein the
2	RSV NS1 and NS2 genes are both deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	138. The isolated polynucleotide molecule of claim 130, wherein the
2	RSV SH and NS2 genes are both deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	139. The isolated polynucleotide molecule of claim 130, wherein the
2	RSV SH, NS1 and NS2 genes are all deleted to form the recombinant RSV genome or
3	antigenome or antigenome.
1	140. The isolated polynucleolide molecule of claim 128, wherein said
2	displacement polynucleotide(s) is/are added, substituted, or rearranged within the
3	recombinant RSV genome or antigenome to cause a positional shift of said one or more
4	shifted RSV gene(s) or genome segment(s) within said recombinant genome or
5	antigenome to a more promoter-proximal or promoter-distal position relative to a position
6	of said RSV gene(s) or genome segment(s) within a wild type RSV genome or
7	antigenome.
1	141. The isolated polynucleotide molecule of claim 140, wherein said
2	displacement polynucleotide(s) added, substituted, or rearranged within the recombinant
3	RSV genome or antigenome comprise(s) one or more RSV NS1, NS2, SH, M2(ORF2), F,

and/or G gene(s) or genome segment(s) thereof.

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RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or

The isolated polynucleotide molecule of claim 144, wherein both

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type gene order position of F.

3	ant\senome to gene order positions that are more promoter-proximal compared to the	
4	wild type gene order positions of G and F.	
1	150. The isolated polynucleotide molecule of claim 149, wherein the	
2	RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein	
73	gene F is shifted to gene order position 2 within said recombinant RSV genome or	
4	antigenome	
1	151. The isolated polynucleotide molecule of claim 144, wherein one or	
2	more RSV NS1 NS2, SH, M2(ORF2), or G gene(s) or genome segment(s) thereof is/are	
3	deleted in the recombinant RSV genome or antigenome.	
1	152. The isolated polynucleotide molecule of claim 144, wherein a	
2	displacement polynucleotide comprising a RSV NS1 gene is deleted to form the	
3	recombinant RSV genome or antigenome.	
1	153. The isolated polynucleotide molecule of claim 144, wherein a	
2	displacement polynucleotide comprising a RSV NS2 gene is deleted to form the	
3	recombinant RSV genome or antigenome.	
1	154. The isolated polynucleotide molecule of claim 144 wherein a	
2	displacement polynucleotide comprising a RSV SH gene is deleted to form the	
3	recombinant RSV genome or antigenome.	
1	155. The isolated polynucleonide molecule of claim 154, wherein the	
2	RSV glycoprotein gene G is rearranged within said recombinant RSV genome or	
3	antigenome to a gene order position that is more promoter-proximal compared to the wile	
4	type gene order position of G.	
1	156. The isolated polynucleotide molecule of claim 155, wherein the	
2	RSV glycoprotein gene G is shifted to gene order position 1 within said recombinant RSV	
3	genome or antigenome.	
1	157. The isolated polynucleotide molecule of claim 154, wherein the	
2	RSV glycoprotein gene F is rearranged within said recombinant RSV genome or	

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antigenome to a gene order position that is more promoter-proximal compared to the wild

antigenome or antigenome.

	•			
1	158. The isolated polynucleotide molecule of claim 157, wherein the			
2	RSV glycoprotein gene F is shifted to gene order position 1 within said recombinant RSV			
3	genome or antigenome.			
1	\\\159. The isolated polynucleotide molecule of claim 158, which is			
7	F1/ΔSH.			
1	160. The isolated polynucleotide molecule of claim 154, wherein both			
2	RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or			
3	antigenome to gene order positions that are more promoter-proximal compared to the			
4	wild type gene order positions of G and F.			
1	161. The isolated polynucleotide molecule of claim 160, wherein the			
2	RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein			
3	gene F is shifted to gene order position 2 within said recombinant RSV genome or			
4	antigenome.			
1	162. The isolated polynucleotide molecule of claim 144, wherein the			
2	RSV SH and NS2 genes are both deleted to form the recombinant RSV genome or			
3	antigenome or antigenome.			
1	163. The isolated polynucleotide molecule of claim 162, wherein both			
2	RSV glycoprotein genes G and F are real ranged within said recombinant RSV genome or			
3	antigenome to gene order positions that are more promoter-proximal compared to the			
4	wild type gene order positions of G and F.			
1	164. The isolated polynucleoride molecule of claim 163, wherein the			
2	RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein			
3	gene F is shifted to gene order position 2 within said recombinant RSV genome or			
4	antigenome.			
1	165. The isolated polynucleotide molecule of claim 164, wherein the			
2	RSV SH, NS1 and NS2 genes are all deleted to form the recombinant RSV genome or			

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1	166. The isolated polynucleotide molecule of claim 165, wherein both				
2	RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or				
3	antigenome to gene order positions that are more promoter-proximal compared to the				
4	wild type gene order positions of G and F.				
1	167. The isolated polynucleotide molecule of claim 166, wherein the				
2	RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein				
3	gene F is shifted to gene order position 2 within said recombinant RSV genome or				
4	antigenome.				
1	168. The isolated polynucleotide of claim 124, wherein the recombinant				
2	genome or antigenome comprises a partial or complete human or bovine RSV				
3	background genome or antigenome combined with one or more heterologous gene(s)				
4	and/or genome segment(s) from a different RSV to form a human-bovine chimeric				
5	genome or antigenome.				
1	169. The isolated polynucleotide of claim 168, wherein one or both				
2	human RSV glycoprotein genes F and G is/are substituted to replace one or both				
3	counterpart F and G glycoprotein genes in a partial bovine RSV background genome or				
4	antigenome.				
1	170. The isolated polynucle tide of claim 169, wherein both human				
2	RSV glycoprotein genes F and G are substituted to replace counterpart F and G				
3	glycoprotein genes in the bovine RSV background genome or antigenome.				
1	171. The isolated polynucleotide of claim 168, wherein one or more				
1					
2	human RSV glycoprotein genes selected from F, G and SH is/are added or substituted at a				
3	position that is more promoter-proximal compared to a wild-type gene order position of a				
4	counterpart gene or genome segment within a partial or complete bovine RSV				
5	background genome or antigenome.				
1	172. The isolated polynucleotide of claim 171, wherein both human				



RSV glycoprotein genes G and F are substituted at gene order positions 1 and 2,

respectively, to replace counterpart G and F glycoprotein genes deleted at wild type

positions 7 and 8, respectively in a partial bovine RSV background genome or antigenome.

173. The isolated polynucleotide of claim 124, wherein the recombinant genome or antigenome is further modified by addition or substitution of one or more additional heterologous gene(s) or genome segment(s) from a human RSV within the partial or complete povine background genome or antigenome to increase genetic stability or alter attenuation, reactogenicity or growth in culture of the recombinant virus.

- 174. The isolated polynucleotide molecule of claim 124, wherein the recombinant genome or antigenome incorporates antigenic determinants from both subgroup A and subgroup B human RSV.
- 175. The isolated polynucleotide molecule of claim 124, wherein the recombinant genome or antigenome is further modified by incorporation of one or more attenuating mutations.
- 176. The isolated polynucleotide molecule of claim 124, wherein the recombinant genome or antigenome is further modified by incorporation of a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.
- 177. The isolated polynucleotide molecule of claim 176, wherein a SH, NS1, NS2, M2ORF2, or G gene is modified.
- 178. The isolated polynucleotide molecule of claim 177, wherein the SH, NS1, NS2, M2 ORF2, or G gene is deleted in whole or in part or expression of the gene is ablated by introduction of one or more stop codons in an open reading frame of the gene.
  - 179. The isolated polynucleotide molecule of claim 176, wherein the nucleotide modification comprises a nucleotide deletion, insertion, addition or rearrangement of a cis-acting regulatory sequence of a selected RSV gene within the recombinant RSV genome or antigenome.

1	180. The isolated polynucleotide molecule of claim 124, wherein said			
2	displacement polynucleotide(s) comprise(s) one or more deletion(s) within a			
3	nontranslated sequence at the beginning or end of an RSV open reading frame or in an			
4	intergenic region or 3' leader or 5' trailer portion of the RSV genome.			
1	181. The isolated polynucleotide molecule of claim 180, wherein said			
2	displacement polynucleotides comprise or partial gene deletion.			
1	182. The isolated polynucleotide molecule of claim 181, wherein said			
2	partial gene deletion is a partial deletion of the SH gene.			
1	183. The isolated polynucleotide molecule of claim 182, wherein said			
2	partial deletion of the SH gene comprises a deletion within the SH downastream non-			
3	translated region.			
1	184. The isolated polynucleotide molecule of claim 183, which is RSV			
2	6120 having a deletion of 112 nucleotides at positions 4499-4610 in the recombinant			
3	RSV antigenome.			
1 .	185. The isolated polynucleotide molecule of claim 124, wherein said			
2				
	displacement polynucleotide(s) is/are selected from one or more region(s) of a			
3	downstream untranslated sequence of an RSV gene.			
1	186. The isolated polynucleotide molecule of claim 185, wherein said			
2	downstream untranslated sequence(s) is/are from NS1 (positions 519-563), NS2			
3	(positions 1003-1086), P (positions 3073-3230), M (positions 4033-4197), F(positions			
4	7387-7539), and/or M2 (positions 8433-8490) genes			
1	187. The isolated polynucleotide molecule of claim 124, wherein said			
2	displacement polynucleotide(s) is/are selected from one or more region(s) of a upstream			
3	untranslated sequence of an RSV gene.			
1	188. The isolated polynucleotide molecule of claim 187, wherein said			
2	one or more upstream untranslated sequences is/are from NS1 (positions 55-96), NS2			

(positions 606-624) and/or SH (positions 4231-4300).

1	1	89.	The isolated polynucleotide molecule of claim 124, wherein said			
2	displacement polynucleotide comprises a deletion of nucleotides 4683 to 4685 of the RSV					
3	G gene.					
	\ .	.00				
1	\	190.	The isolated polynucleotide molecule of claim 124, wherein said			
72	displacement polynucleotide(s) is/are selected from one or more RSV intergenic					
3	sequences.	\				
1	1	194.	The isolated polynucleotide molecule of claim 124, wherein said			
2	displacement po	olynuc	eleotide(s) is/are selected from nucleotides within the RSV 5' trailer			
3	region.	/	<b>、</b>			
1		192.	The isolated polynucleotide molecule of claim 191, wherein a			
2	•		er region that immediately follows the L gene is reduced in size by			
3	75 nucleotides,	100 n	ucleothdes, 125 nucleotides, or more, leaving intact the 5' genomic			
4	terminus.					
1	1	93.	The isolated polynucleotide molecule of claim 124, wherein said			
			\ 1			
2	-	nymuc	eleotide(s) is/are selected from nucleotides within the RSV 3' leader			
3	region.					
1	1	94.	The isolated polynucleotide molecule of claim 193, wherein a			
2	portion of the 3	' traile	er region that excludes a core portion of the viral promoter located			
3	within the first	11 nuc	cleotides of the 3' leader is deleted.			
1	1	95.	The isolated polynucleotide molecule of claim 124, wherein a			
2			eletion from one or any combination of the RSV NS1, NS2, SH, F			
3	•		ds an adjustable reduction in genome length of between 1-806			
4	nucleotides.	- ,				
•	naoreo naos.					
1	1	96.	The isolated polynucleotide molecule of claim 124, wherein a			
2	partial or compl	ete de	eletion from one or any combination of RSV intergenic regions			

yields an adjustable reduction in genome length of between 1 \ 198 nucleotides.

\	197.	The isolated polynucleotide molecule of claim 124, wherein a			
partial or co	omplete d	leletion from one or any combination of RSV intergenic regions			
yields an ac	yields an adjustable reduction in genome length of between 1-198 nucleotides.				
\					
	198.	A method for producing an infectious attenuated recombinant RSV			
particle from	m one or	more isolated polynucleotide molecules encoding said RSV,			
comprising	: \				
	expre	ssing in a cell or cell-free lysate an expression vector comprising an			
isolated pol	lynucled	ide comprising a recombinant RSV genome or antigenome having			
one or more	e shifted	RSV gene(s) or genome segment(s) within said recombinant genome			
		s/are positionally shifted to a more promoter-proximal or promoter-			
•		we to a position of said RSV gene(s) or genome segment(s) within a			
		me or antigenome, and RSV N, P, L and RNA polymerase elongation			
factor prote					
•					
	199.	The method of claim 198, wherein the recombinant RSV genome			
or antigeno	me and th	ne N, P, L and RNA polymerase elongation factor proteins are			
expressed b	y two or	more different expression vectors.			
	200.	An isolated infectious chimeric respiratory syncytial virus (RSV)			
comprising	a major i	nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large			
polymerase	protein (	L), a RNA polymerase elongation factor, and a partial or complete			
bovine RSV	backgro	ound genome or antigenome combined with a plurality of			
heterologou	is gene(s)	and/or genome segment(s) of a human RSV selected from			
heterologou	is gene(s)	and/or genome segment(s) of RSV NS1, NS2, M, SH, G, and/or F,			
to form a h	uman-bov	vine chimeric RSV genome or antigenome.			
	201.	The isolated infectious RSV of claim 200, wherein both human			
NS1 and N	S2 genes	are substituted for their bovine counterpart NS1 and NS2 genes.			
	202.	The isolated infectious RSV of claim 20, which is rBRSV/A2-			
NS1+2.					
	203.	The isolated infectious RSV of claim 200, wherein human NS1,			

NS2, G, and F are substituted for their bovine counterpart NS1, NS2, G and F genes.

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1 204. The isolated infectious RSV of claim 203, which is rBRSV/A2-2 NS1+20E

203: The isolated infectious RSV of claim 200, wherein human M, SH, G, and F are substituted for their bovine counterpart M, SH, G and F genes.

The isolated infectious RSV of claim 203, which is rBRSV/A2-206. MSHGF.

An isolated polynucleotide molecule comprising a recombinant 207. RSV genome or antigenome comprising a partial or complete bovine RSV background genome or antigenome combined with a plurality of heterologous gene(s) and/or genome segment(s) of a human RSV selected from heterologous gene(s) and/or genome segment(s) of RSV NS1, NS2, M, SH, G, and/or F genes, to form a human-bovine chimeric RSV genome or antigenome.